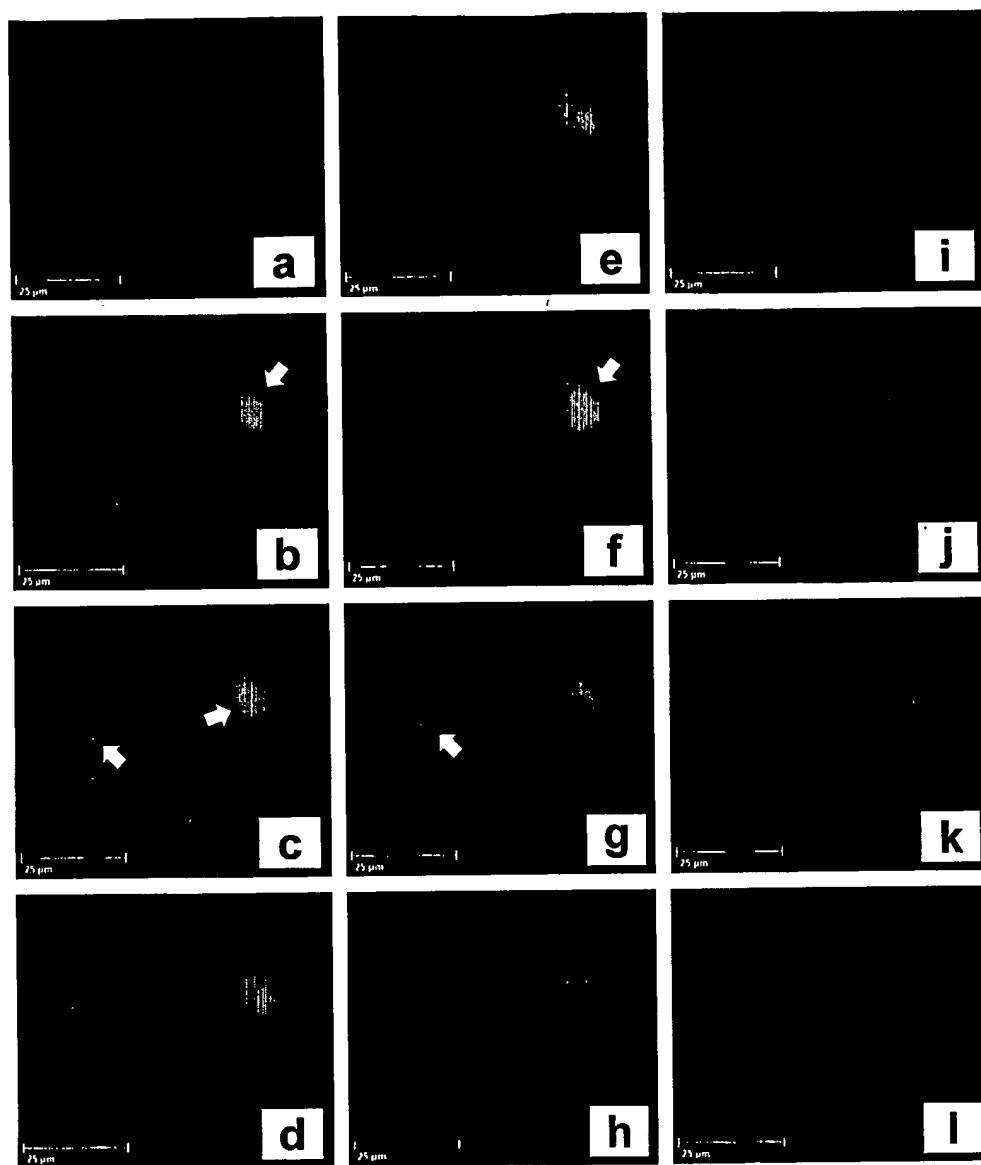
**FIG. 1**

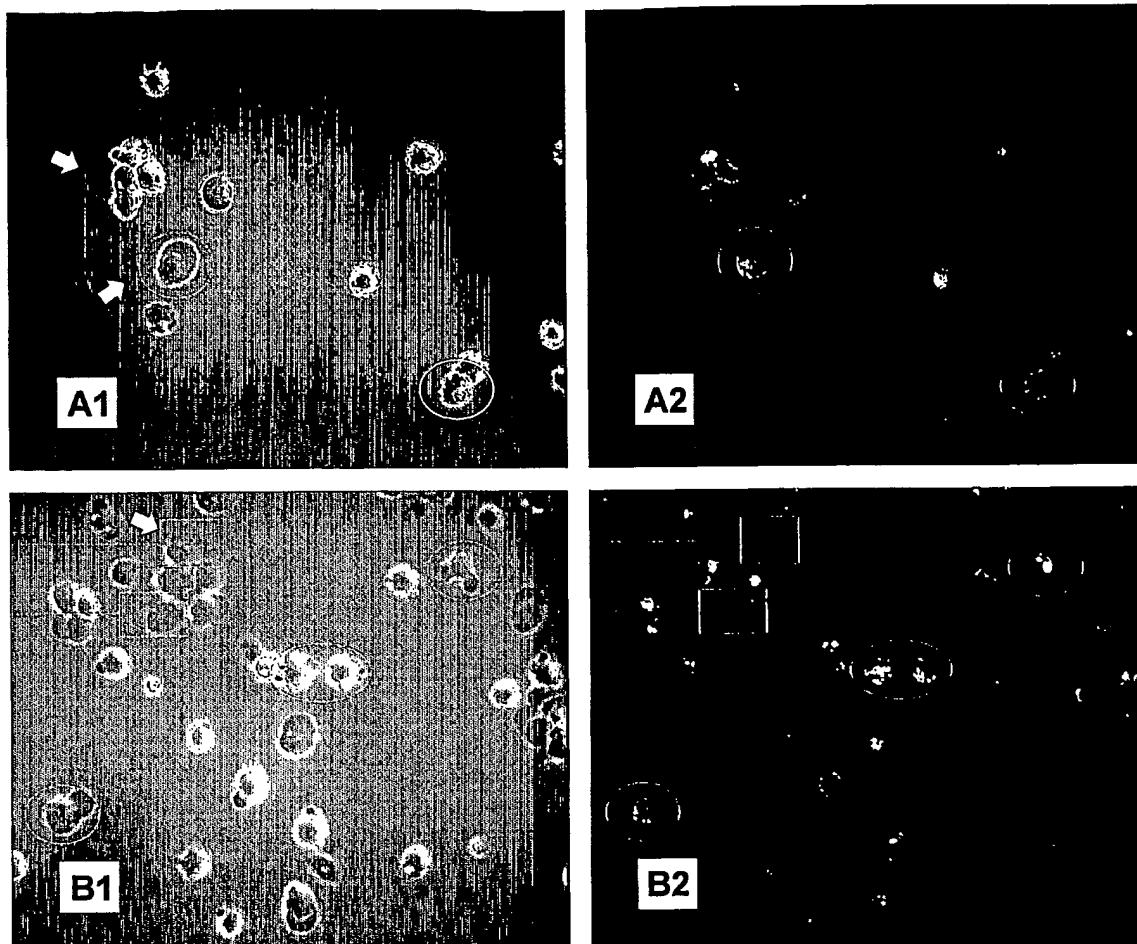
Basic morphological appearance of human myeloid dendritic cells (mDCs) during differentiation *in vitro*.

NOT AVAILABLE COPY



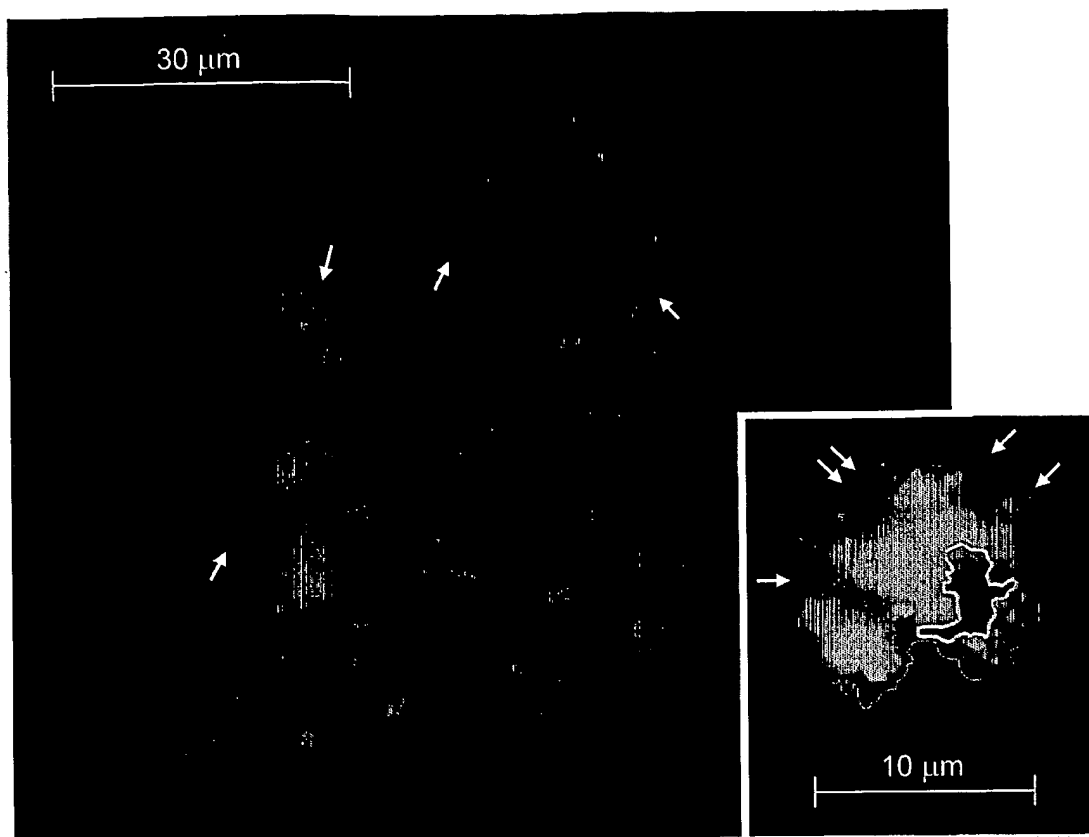
Serial Optical sections through immature myeloid dendritic cells (mDCs) targeted with *fucose-labeled* liposomes delivering the tracer dye calcein.

FIG. 2

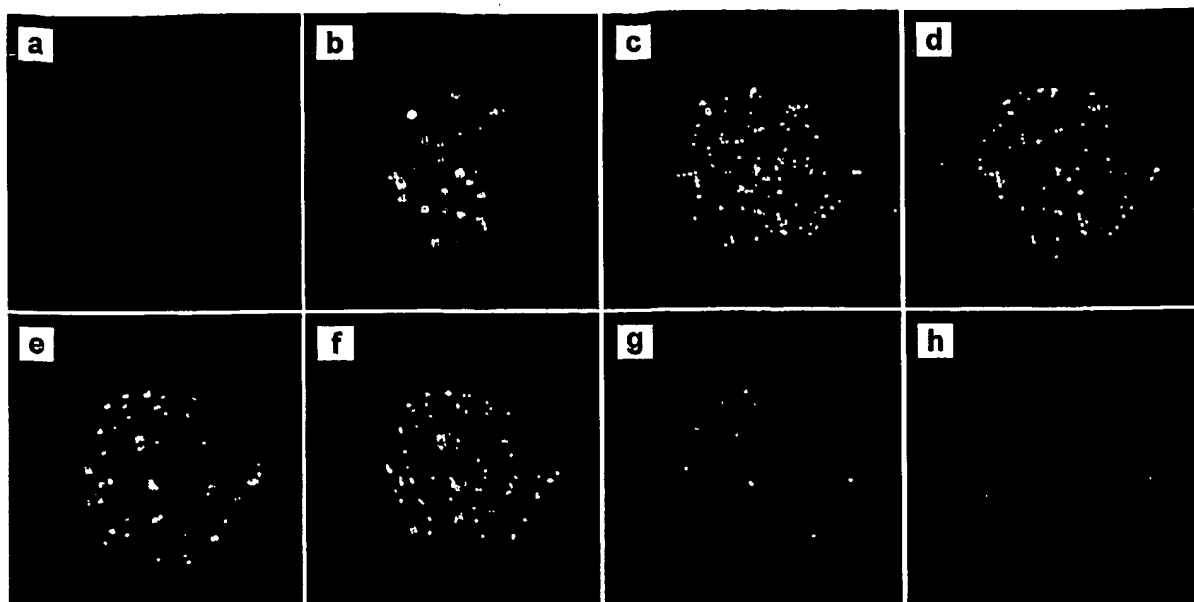


Binding and uptake of *mannose-labeled* liposomes by immature mDCs after 5 days of culture.

FIG. 3

**FIG. 4**

C-type lectin-specific targeting of clustered mature mDCs.



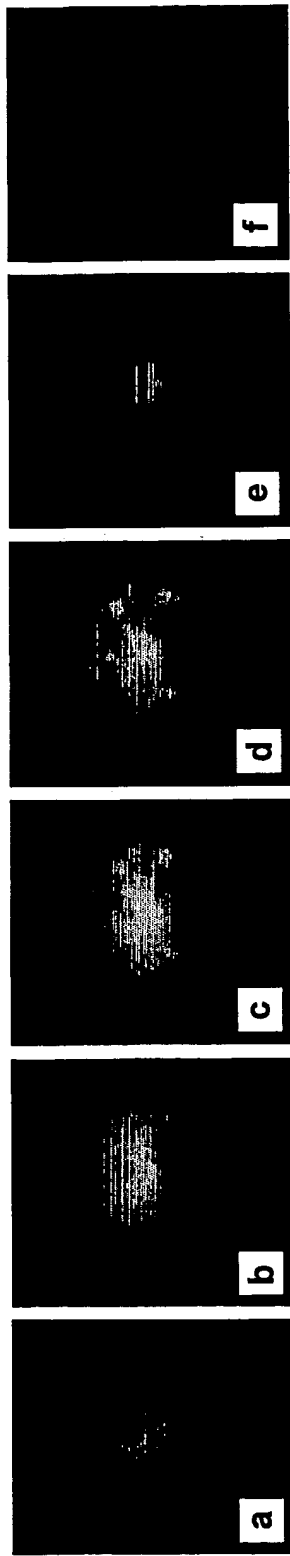
Binding and uptake of *fucose-labeled* liposomes by human macrophages after 7 days of culture.

FIG. 5



Color fluorescence photomicrograph of a representative macrophage from a different donor 2 hours after targeting with *fucose-labeled* liposomes.

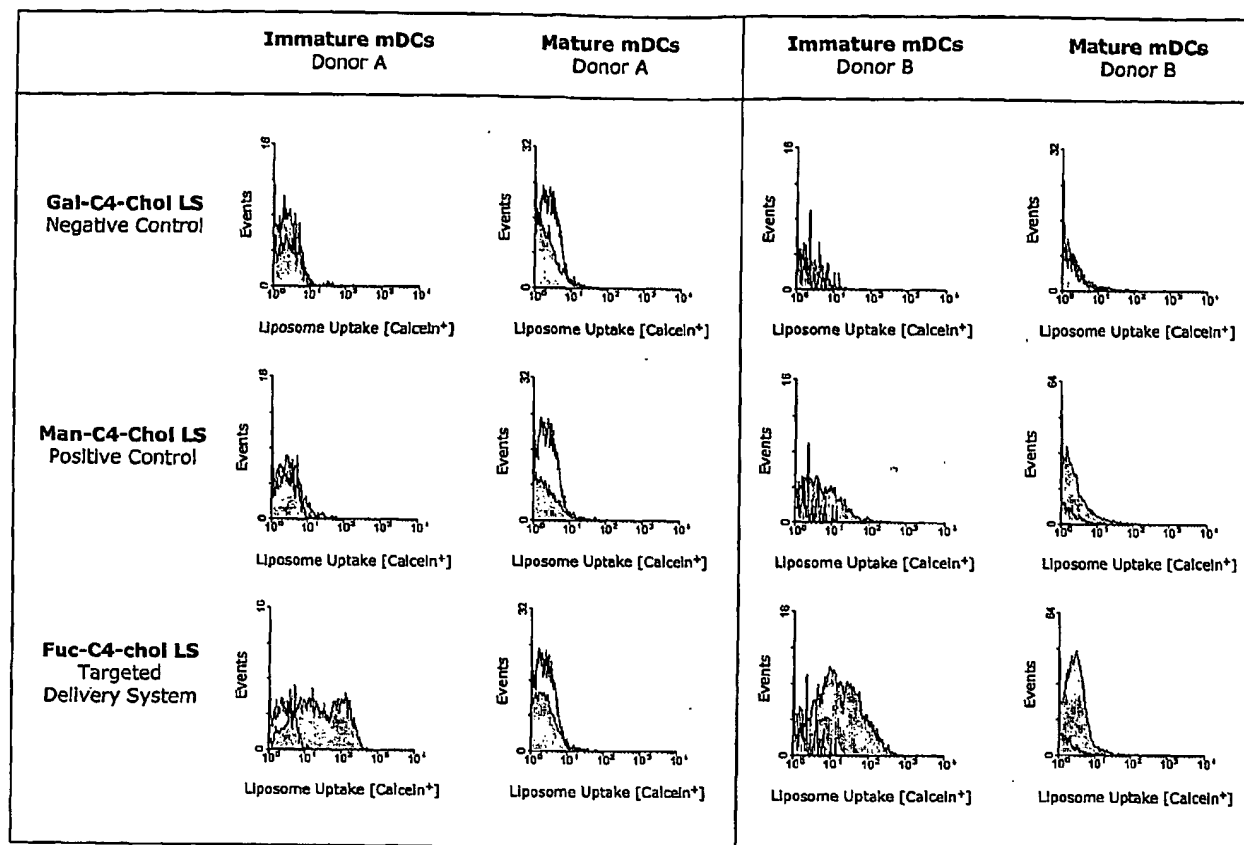
FIG. 6



Serial optical sections through a monocyte targeted with *Fuc-4C-Chol*-labeled liposomes delivering the tracer dye calcein.

Fig. 7

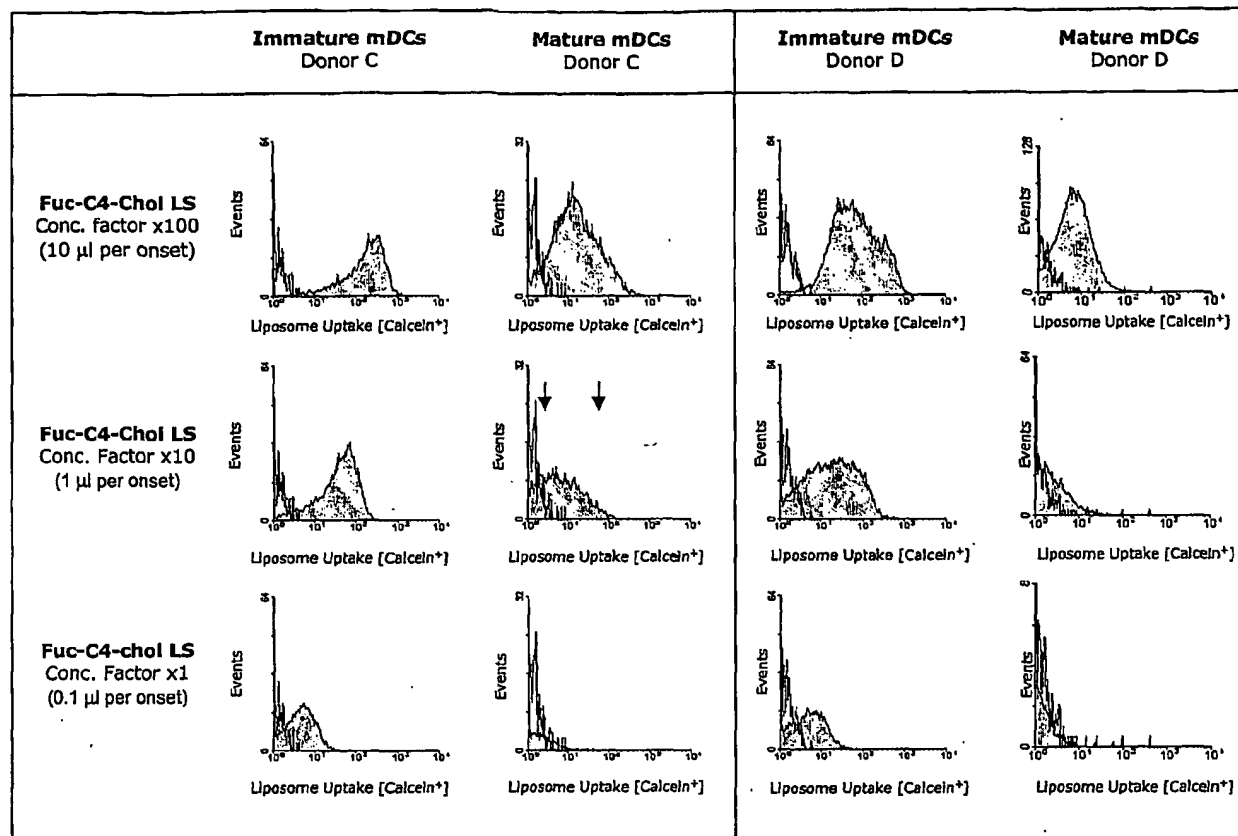
7/13



The fucose-targeted compound delivery system is highly specific and has an extremely high targeting efficacy.

FIG. 8

8/13

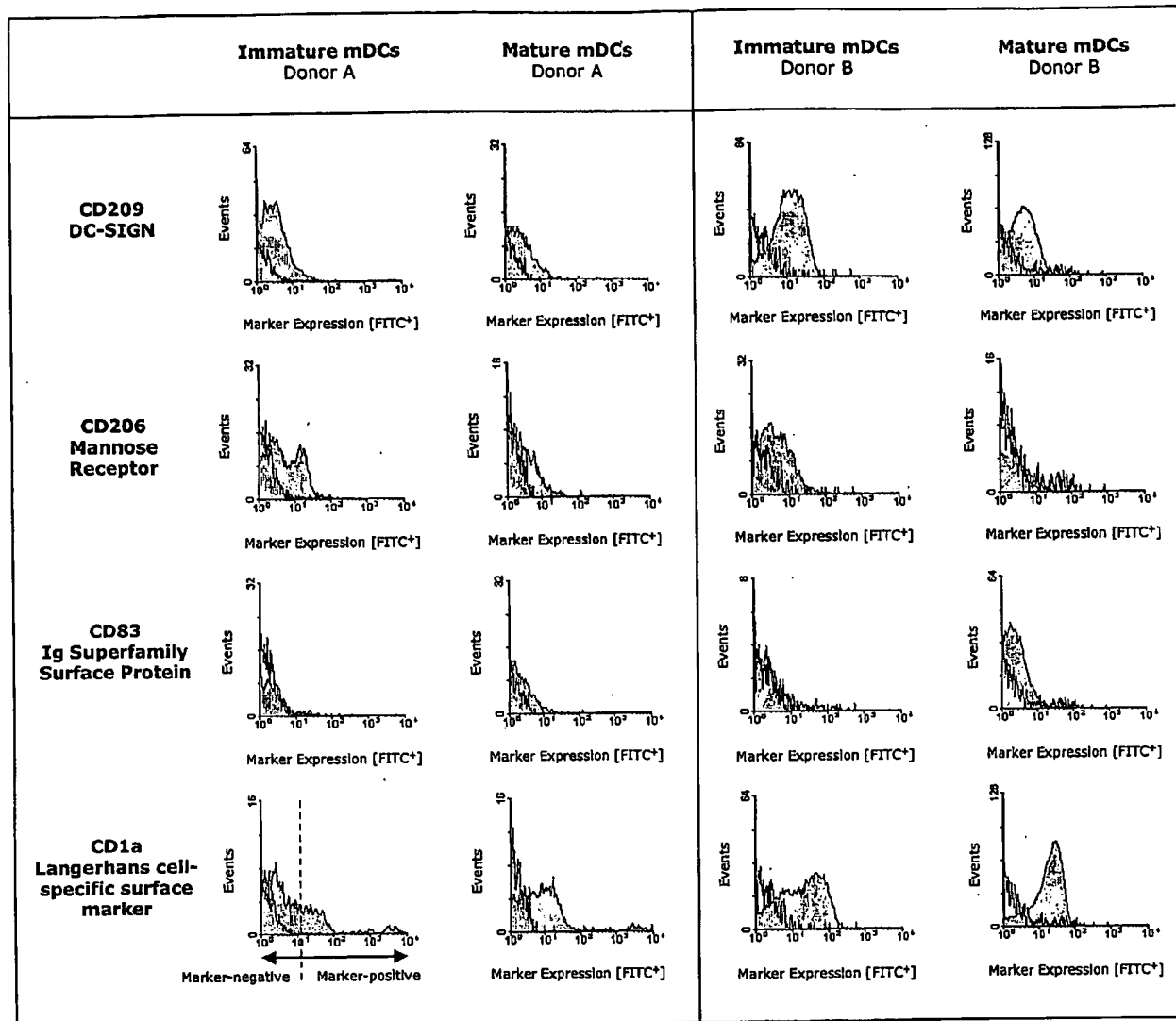


Increased concentrations of fucose-labeled liposomes targets both immature and mature mDCs highly efficiently.

FIG. 9



9/13

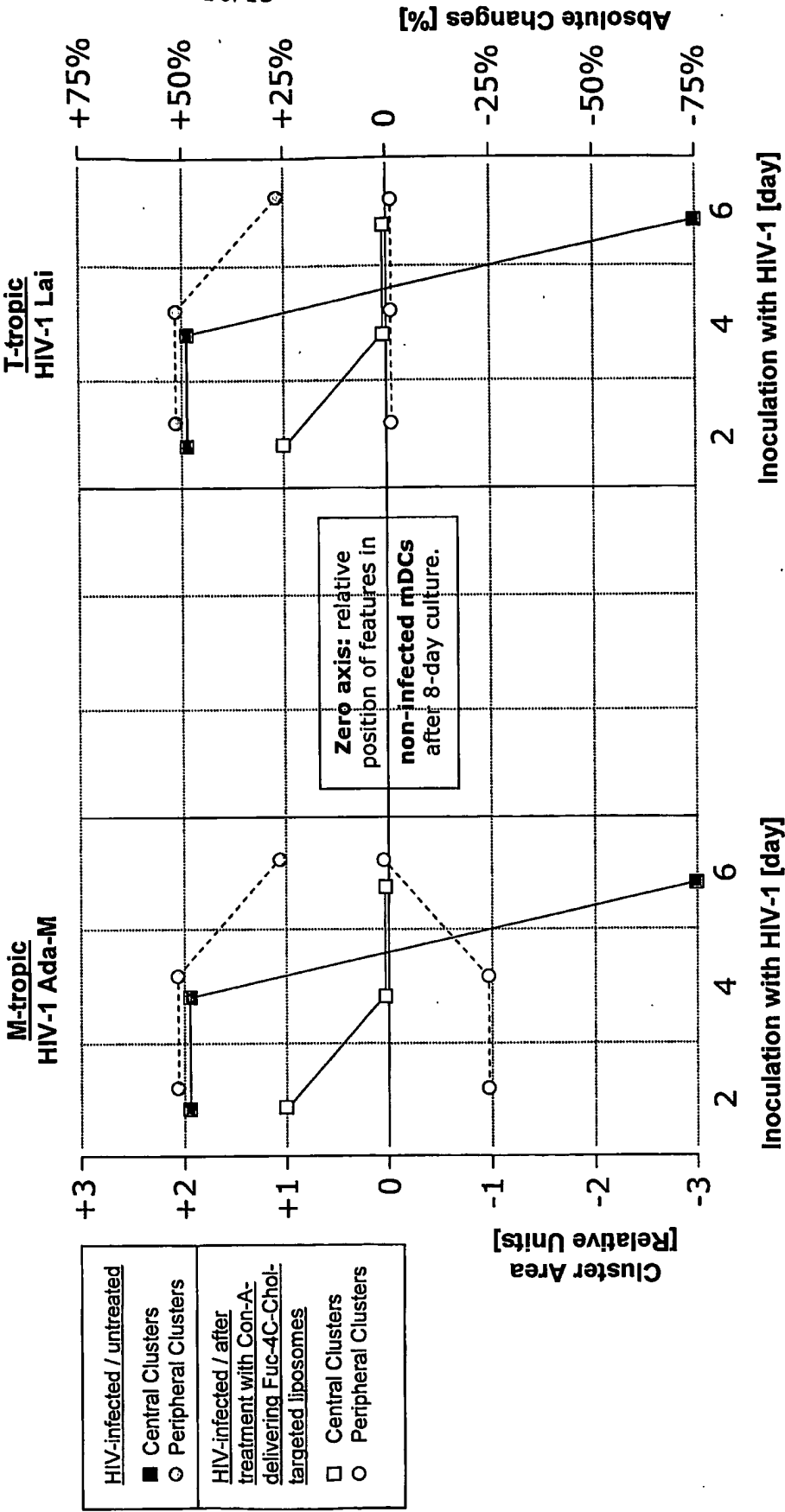


Phenotyping of immature and mature myeloid dendritic cells.

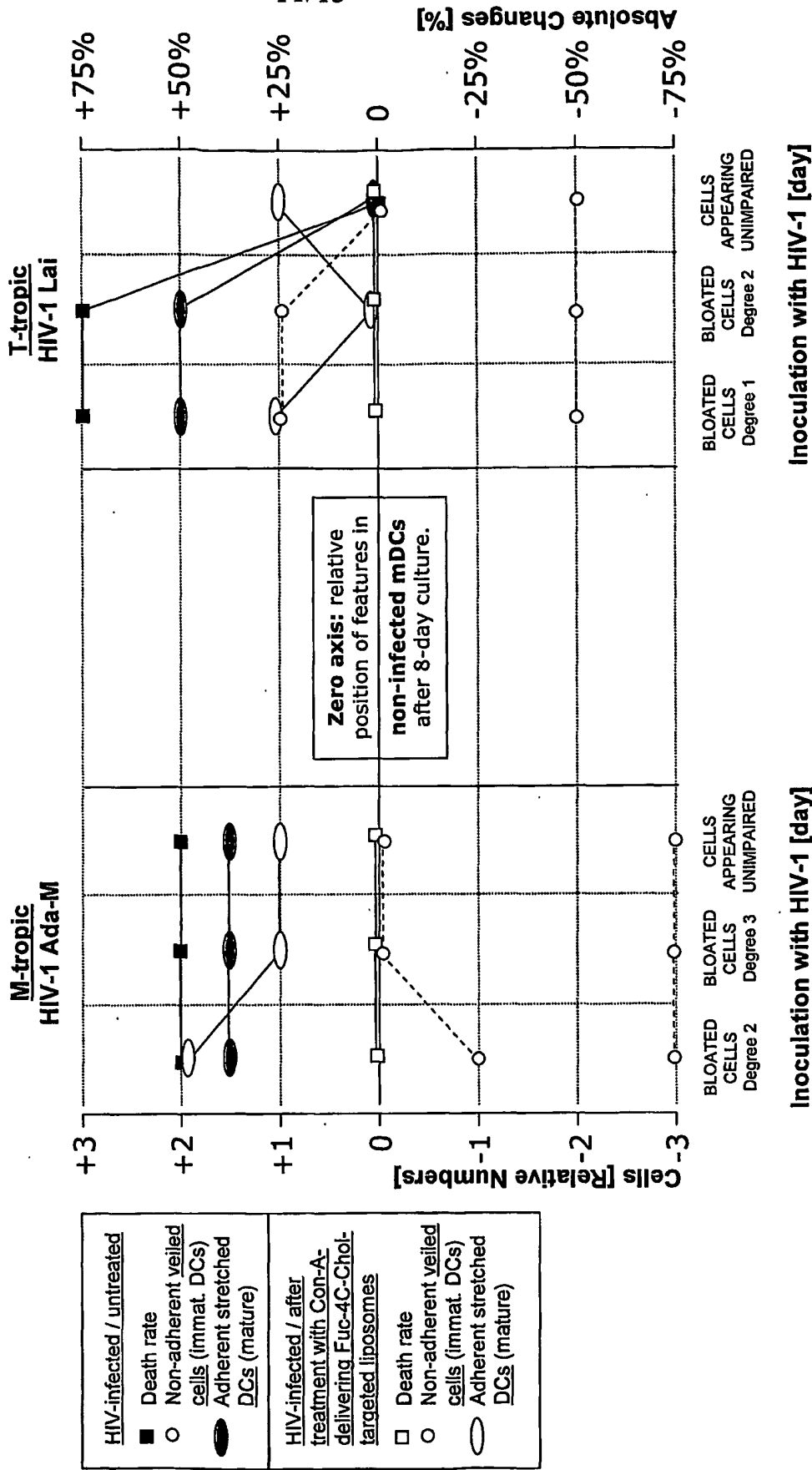
FIG. 10

10/13

**FIG. 11**  
Morphological changes in mDCs after 8-day culture of HIV-infected mDCs upon or without targeted treatment. I. Culture appearance and homotypic mDC clustering.



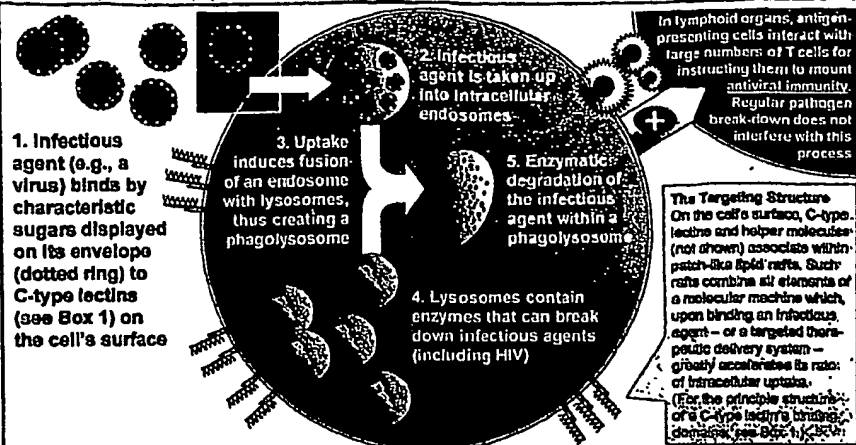
**FIG. 12**  
Morphological changes in mDCs after 8-day culture of HIV-infected mDCs upon or without targeted treatment. II. Types of mDCs and viability.



12/13

**Fig. 13.** (I) Normal Pathogen Elimination, (II) Evasion by HIV, and (III) The Inventive Carbohydrate-Lectin Targeting and Treatment System.**I. Normal Destruction of an Infectious Agent**

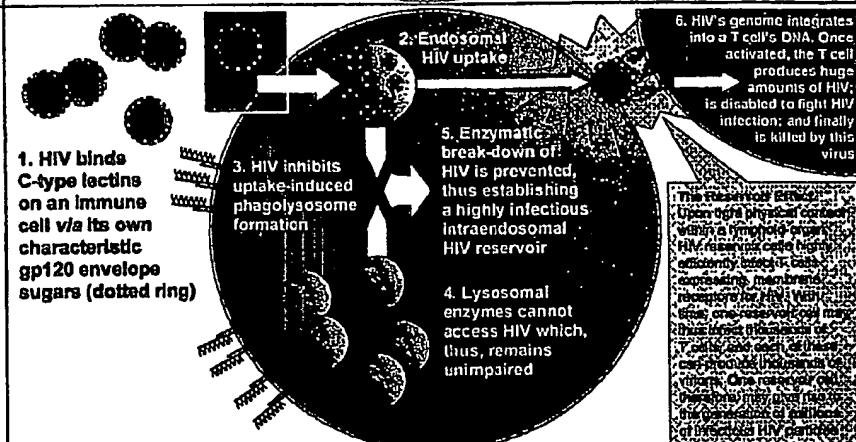
In the human immune system, the first cells recognizing infectious agents are antigen-presenting cells (dendritic cells, macrophages, and others). Normally, these cells digest and dismantle infectious agents presenting their fragments to T cells for induction of specific immunity. The large circle represents such a cell, as well as key processes involved in the recognition and destruction of infectious agents. The cell section on the upper right depicts a T cell instructed for action.

**II. Evasion of Destruction by HIV and Formation of a Chronic HIV Reservoir**

HIV reservoir populations can retain highly infectious virus for prolonged, yet different periods of time, i.e.,

- Days to months (dendritic cells);
- Months (follicular dendritic cells);
- Months to years (macrophages);
- Years (T-memory cells)

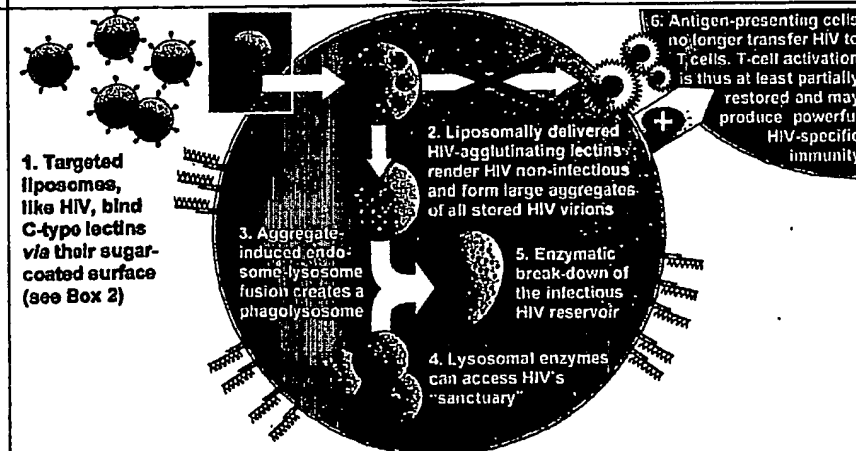
Dendritic cells, with their high turnover rate, and their many physiologic subsets, and their extremely tight and frequent physical interaction with T cells, strike as the most virulent HIV reservoir when compared to the other reservoir cells.

**III. Elimination of the HIV Reservoir: a Two-Step Process Mediated by Carbohydrate-Lectin Interaction****1<sup>st</sup> Level:**

Specific liposomal targeted delivery to the reservoir cell's surface lectins, with subsequent endosomal uptake of the liposomes;

**2<sup>nd</sup> Level:**

Delivery of liposomally encased HIV-agglutinating lectins into the endosomes leads to the break-down of the infectious endosomal HIV reservoir



**Box 1: Cellular Targeting Structure**  
Carbohydrate (Sugar) Recognition Domain (CRD) of a C-Type Lectin

C-type lectin-like domains expressed by T-memory and NK HIV-reservoir cells also bear CRDs and thus can be targeted, too

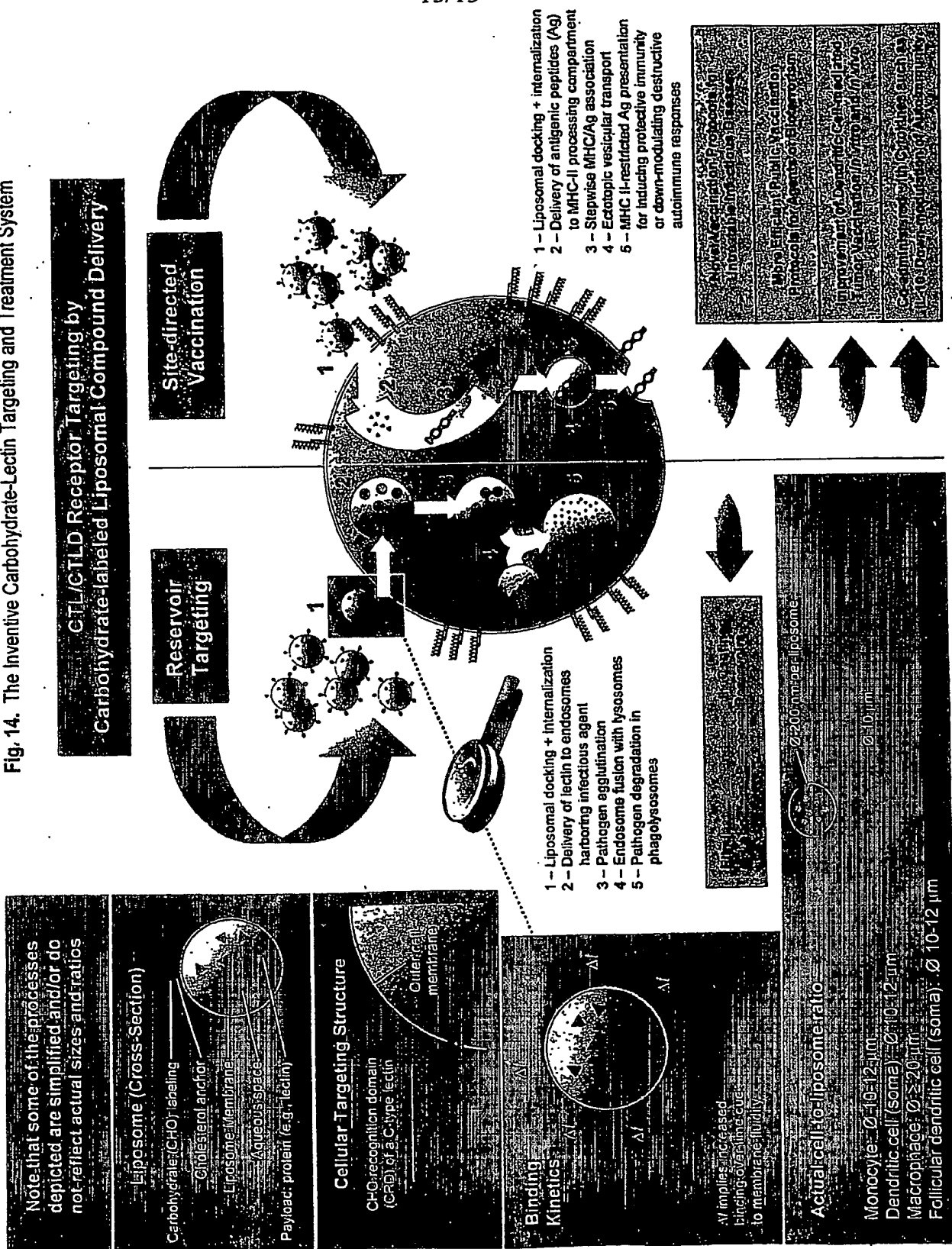
**Box 2: Liposomal Targeting & Delivery System**

Carbohydrate (Sugar) Labeling  
Cholesterol Membrane Anchor  
Liposome Membrane  
Aqueous Interior  
Therapeutic Payload (Lectin)

Note that some of the processes depicted are simplified and/or do not reflect actual sizes and ratios

13/13

Fig. 14. The Inventive Carbohydrate-Lectin Targeting and Treatment System



**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record.**

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☒ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☒ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**